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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,441	03/08/2004	Michael Radomsky	DEPYP003D1C1	1814

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,441	RADOMSKY, MICHAEL	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/06/09 has been entered.

The following office action is a responsive to the Amendment filed, 04/06/09.

The amendment filed 04/06/09 affects the application, 10/796,441 as follows:

Claim 21 has been amended. The rejection made under 35 U.S.C. 103(a) of the prior office action mailed 02/04/09 is maintained.

1. The responsive to applicants' amendment is contained herein below.

Claims 21-22 are pending in application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brekke et al. (WO 9409722).

In claim 21, applicant claims "A method of treating diseased, injured or abnormal bone at a tissue site of desired bone growth comprising the step of applying onto said site an injectable liquid composition comprising an effective amount of a mixture of hyaluronic acid, growth

factor bFGF and excipients to maintain biological activity of said factor, said composition being sufficient to enhance bone growth rate and magnitude and having a viscosity and biodegradability sufficient to persist at said site for a period of time sufficient to enhance said bone growth rate and magnitude." Claim 22 is drawn to a method according to claim 21 wherein said bFGF is present in a range of about 10^{-6} to 100 mg/ml in said composition.

Brekke et al. disclose a composition for treating bone such as abnormal bone at a tissue site of desired bone growth (e.g., the voids in bone) comprising the step of applying to said site a composition comprising a mixture of hyaluronic acid, growth factor bFGF and excipients, and wherein the said composition can promote (enhance) bone growth (see abstract, page 4, line 20 to page 7, line 11 and especially page 6 the paragraph numbered as 4; also see claims). In addition, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone.

The difference between applicant's claimed method and the method taught by Brekke et al. is that Brekke et al. does not exemplify the use of said composition, per se.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the method suggested by Brekke et al. to treat abnormal, injured or diseased bone by injecting or applying to the tissue site of said abnormal, injured or diseased bone (wherein Brekke et al.'s macro and micro-structure complex have been inserted) a solution or liquid composition comprising an effective amount of a mixture of hyaluronic acid, a growth factor and excipients such as water and to alter the viscosity of said composition depending on factors such as the severity of the bone condition or disorder and the individual that is being treated.

One having ordinary skill in the art would have been motivated to use the method suggested by Brekke et al. to treat abnormal, injured or diseased bone by injecting or applying to the tissue site of said abnormal, injured or diseased bone (wherein Brekke et al.'s macro and micro-structure complex have been inserted) a solution or liquid composition comprising an effective amount of a mixture of hyaluronic acid, a growth factor and excipients such as water and to alter the viscosity of said composition depending on factors such as the severity of the bone condition or disorder and the individual that is being treated. It should also be noted that use of specific concentration of the components (such as bFGF) of said composition also depending on factors such as the severity of the bone condition or disorder and the individual that is being treated.

Response to Arguments

Applicant's arguments with respect to claims 21 and 22 have been considered but are not found convincing.

The applicant argues that Brekke's must have structural competence, that is, a gross structure to provide a mechanical support and structural surface for the dynamic biological processes for genesis, growth and development of new non-calcified and calcified connective tissue. This function is served by the biologically acceptable, biodegradable solid polymer (such as polylactic acid) arranged as a one piece porous solid body with enclosed randomly sized, randomly positioned and randomly shaped interconnecting voids, each void communicating with all of the others, and communicating with substantially the entire exterior of the body. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone.

Applicant argues that there must be a microstructure composed of the solid chemotatic ground substance, which can be hyaluronic acid. The hyaluronic acid is used as a solid material,

a velour composed of fibrils with intercalated voids of microscopic dimensions. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone.

The applicant argues that Brekke requires the osteoinductive/osteogenic substance which is a growth factor. These requirements dictate the use of a solid composition as shown in Brekke's FIGS. 1-6, and described on page 20, lines 18-26. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a

carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone.

The applicant argues that the examiner points out that hyaluronic acid as a gel may be injected into the solid porous polylactic acid block. Brekke, page 20, lines 11-13. But the block is not a tissue site. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone. It should be noted that site of desired bone growth is considered a tissue site.

The applicant argues that the injectable composition, containing only HA and perhaps a diluent, does not contain all the necessary components of the injectable composition recited in the present claims. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical

binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution (including excipients such as water) at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone. It should be noted that the said injectable composition suggested by Brekke et al. does contain all the required components.

The applicant argues that the fact that two of the components, HA and the growth factor, can exist separately as injectable compositions prior to their use does not lead one to combine both of them onto an injectable composition to a tissue site of desired bone growth. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the

osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution (including excipients such as water) at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone.

The applicant argues that it is submitted that the teaching of the methods in Brekke to one of ordinary skill in the art would be that in order to induce the growth of bone, one needs the solid macrostructure, and possibly also the solid microstructure, of the device in Brekke. This is a teaching away from the presently claimed method applying an injectable liquid composition containing all of the recited components onto a tissue site of desired bone growth. However as set forth in the above rejection, Brekke et al. disclose that hyaluronic acid is a carrier for Osteoinductive/Osteogenic Agent(s) and that by chemical binding, as well as by mechanical entrapment, hyaluronic acid is capable of being joined to osteoinductive/osteogenic agents such as the bone morphogenetic protein (BMP) and the bone-derived growth factor (BDGF) (page 13 the paragraph numbered as 3). Furthermore, Brekke et al. disclose that their osteoinductive/osteogenic substance or growth factor can be injected as a solution (see page 19, last paragraph to page 20, 1st paragraph). This suggests to one of ordinary skill in the art that hyaluronic acid (that facilitates osteogenesis) as a carrier can be combined with the osteoinductive/osteogenic agents (such as growth factor bFGF) and injected or applied as a solution at the tissue site of desired bone growth (wherein Brekke et al.'s macro and micro-structure complex have been inserted) to treat bone such as an abnormal bone. It should be noted that site of desired bone growth is considered a tissue site. Thus, Brekke et al. do not teach away.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
June 6, 2009.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623